II. Support for the Claims

Support for the revised and new claims exists throughout the specification and claims of the original and parent applications. Any fees deemed necessary for the new claims should be deducted from Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4040.000300.

Claim 1 has been revised to recite that the therapeutic combination product is arranged for delivery of at least one individual inhalable dose of ingredient (a), either together with or separately from ingredient (b), wherein the dose comprises ingredient (a) in an inhalable amount of at least 25mg. This is supported throughout the specification and claims, with particular support in claims 22 and 23.

Claim 22 now recites doses in which ingredient (a) is present in an inhalable amount of at least 40mg, as supported throughout the specification and claims, with particular support in claim 24.

Claims 23 and 24 have been revised to depend from the new claims introduced herein, and to recite that the products of those claims are also arranged for delivery of at least one individual inhalable dose comprising ingredient (a) in an inhalable amount of at least 25mg, which is supported by claims 22 and 23.

Claim 25 now depends from claim 1.

Independent claims 30, 31, 34 and 35 have also been revised as in claim 1, and now recite the delivery of inhalable doses in which ingredient (a) is present in an inhalable amount of at least 25mg, as supported by original claim 23.

New claim 36 is an alternative independent claim defining certain therapeutic combination products of the invention. This is based upon claim 1, but in which ingredient (a) is defined as in claim 2, and wherein ingredients (a) and (b) are provided in a form for separate administration, as in claim 27.

Finally, new claim 37 is another alternative independent claim based upon claims 1 and 36. In addition to defining ingredient (a) as in claim 2, new claim 37 also defines the antiasthma drug as a β_2-agonist, cromone, antimuscarinic drug or leukotriene receptor antagonist, as recited within original claim 14, and further recites that the first and second components of ingredient (a) are present in the weight ratio defined in claim 5.

It will therefore be understood that no new matter is included within any of the revised or new claims.

III. Rejection of Claims 1-35 Under 35 U.S.C. § 103(a)

The Action first rejects claims 1-35 under 35 U.S.C. § 103(a) as allegedly being legally obvious over U.S. Patent No. 4,895,719 to Radhakrishnan *et al.* ("Radhakrishnan") in view of U.S. Patent No. 5,306,483 to Mautone ("Mautone"). Although Applicants respectfully traverse, the rejection is overcome.

The present invention concerns therapeutic combination products, medicaments, packs, delivery devices and associated methods for use in the prevention and/or treatment of asthma. The claims recite a medicament comprising a surface active phospholipid (SAPL) composition, which must be present in finely divided form, and which includes a component that enhances spreading of the medicament over a body surface at about normal mammalian body temperature. The claimed products, packs, methods and medicaments, and certain claimed devices, also comprise an antiasthma drug.

Whilst the antiasthma drug and the SAPL composition may be administered together, for example, as a mixture (*e.g.*, claim 1 and dependent claim 26), the invention also encompasses products in which the antiasthma drug can be administered separately from, simultaneously or sequentially with, the SAPL composition (*e.g.*, claim 1 and dependent claim 27).

Most independent claims recite the delivery of at least one individual inhalable dose that comprises the SAPL composition of ingredient (a) in an inhalable amount of at least 25mg (claims 1-35). The dependent claims variously recite particular features of the invention, such as the components of ingredient (a) (claim 2) and the weight ratios thereof (claims 3-5), certain antiasthma drugs (claims 14 and 17-21) and other doses (claim 22). The other independent claims recite particular SAPL compositions of ingredient (a) (claim 36), optionally in defined weight ratios and in combination with particular antiasthma drugs (claim 37).

As described in detail on pages 3 and 4 of the present specification, the SAPL composition, present in finely divided form, is able on contact with the mucous within the lungs to spread rapidly over the liquid-air interface and some adsorption onto the tissue surface is believed to occur. The binding to the epithelium (shown in the Example; specification at pages 20-25) is believed to mask irritant receptors that elicit the bronchorestrictor reflex. Use of the SAPL composition is thus able to enhance the effectiveness of the antiasthma drug, thought to be a consequence of such protective action[1].

All claims stand rejected under 35 U.S.C. § 103(a) over the combination of Radhakrishnan and Mautone.

The Action first cites certain of the *Graham v. John Deere* factors for an obviousness rejection[2] (page 2), next refers to the Radhakrishnan and Mautone documents separately (pages 2-4) and then concludes that the invention of claims 1-35 is legally obvious (page 2). However, the rejection is based upon a combination of references and the Action does not first provide any reasons to support the proposed combination of references. This is improper.

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[1]It is not a requirement of patentability that an inventor correctly set forth, or even knows, how or why the invention works. *Newman v. Quigg*, 11 USPQ 2d 1340, 1345 (Fed. Cir. 1990). Irrespective of the underlying mechanism, the biological phenomena are shown in the working examples and the specification teaches those of ordinary skill in the art how to make and use the claimed invention.

Before the P.T.O. may combine the disclosure of two or more prior art references in order to establish a *prima facie* case of obviousness, there must be some teaching, suggestion or motivation to combine the references. *In re Rouffet*, 47 USPQ2d 1453, 1456 (Fed. Cir. 1998). Even if every element of an invention can be found in the prior art, obviousness is not established in the absence of sufficient "motivation to combine". *Rouffet* at 1457-1458. A high level of skill in the art cannot be held to substitute for the required motivation to combine. *Rouffet* at 1458.

In the present case, the Office has not set forth evidence sufficient to support the combination of references, and the rejection is therefore *prima facie* improper and should be withdrawn. The following reasoning shows that Radhakrishnan and Mautone would not actually be combined by one of ordinary skill in the art, but even if combined, that the combination does not render the claimed invention legally obvious.

Radhakrishnan concerns the manufacture and use of liposome suspensions, which are said to provide improved controlled release in terms of reduced rapid systemic drug uptake due to free, unencapsulated, drug being present and in terms of modulating delivery of the drug from the administered liposomes. Radhakrishnan thus sets out to provide a structure that will release a drug only slowly at a controlled rate.

In contrast to the slow drug release of Radhakrishnan, Mautone is concerned with achieving rapid spreading over a surface. This is a first line of evidence that the teachings of Radhakrishnan and Mautone are the opposite of each other and the documents are therefore not properly combinable.

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[2]The fourth factor is mis-stated, in that objective evidence concerning non-obviousness does not need to be confined to evidence "present in the application". Evidence of non-obviousness can exist in many sources.

The crystals proposed by Mautone are stated to provide enormous surfaces, *e.g.*, at 200 micrometers^2 for each 0.1 nanogram of phospholipids (Mautone at column 3, lines 44 *et. seq.*). When deposited on an aqueous surface at 37°C in the crystalline form, the combination of Mautone allegedly "instantaneously spreads over the surface as an amorphous surface film carrying with it the therapeutic drug for which it serves as a vehicle" (Mautone at column 3, lines 57 to 61). That behaviour is contrasted by Mautone with the behaviour of liposomes, described at column 3, lines 37 to 44, the probable mode of action of which is stated to be "by adsorption or fusion to the cell surface, whence either the contents may be liberated and enter the cell.....or the entire cell may enter the cell by endocytosis."

Thus, the teaching of Mautone is fundamentally inconsistent with that of Radhakrishnan in that Radhakrishnan is seeking to improve liposome behaviour whilst Mautone is concerned with a form of behaviour which is not liposomal, involving rapid spreading to form an amorphous surface film instead of formation of discrete liposomes. It would thus be counter-intuitive to one skilled in the art to seek to consider the teaching of Mautone with a view to modifying the teaching of Radhakrishnan.

Indeed, as column 3 teaches that liposomes enter cells rather than spreading, Mautone itself clearly teaches against combination with compositions such as those in Radhakrishnan, which are functionally the opposite of the compositions contemplated for use in Mautone. The cited references themselves thus argue against their own combination, which is strong evidence that they would not be considered together by one of ordinary skill in the art.

Assuming for the sake of argument that an artisan reading Radhakrishnan would also consider Mautone, because of the different modes of action of the compositions, which is stressed in Mautone, it would not have been obvious to the ordinary artisan to modify the teaching of Radhakrishnan by using the component ratios of Mautone.

Even if the combination of Radhakrishnan and Mautone was legally proper, the combination would not teach or suggest, to one of ordinary skill in the art at the time the invention was made, the invention defined in the pending claims.

For an obviousness rejection to be proper under 35 U.S.C. § 103, it is required that the cited prior art suggest to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and that the prior art also convey to those of ordinary skill a reasonable expectation of success. *In re Dow Chemical Co.*, 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *Id.*

With regard to claims 1-35, the present application teaches that components of the finely divided SAPL compositions, *i.e.*, powders, bind to the epithelium, giving rise to a protective effect that is of a different origin to that suggested in Mautone. That protective effect contributes to an enhancing of the therapeutic effect of the antiasthma drug. In order to achieve optimum results, however, a relatively large quantity of the SAPL composition should be used to obtain a desired level of binding, such as the 25mg inhalable amounts of claim 1 or the 40mg inhalable amounts of claim 22.

Radhakrishnan does not teach or suggest finely divided SAPL compositions in individual inhalable doses of at least 25mg. Indeed, Radhakrishnan does not recognise any therapeutic effect contributed by the lipid components of their liposomes, the lipids being present only to provide a delivery vehicle. Therefore, there would have been no incentive to one skilled in the art reading Radhakrishnan to optimize the lipid doses, let alone to arrive at the invention of claims 1-35. There is nothing in Mautone to suggest that the use of relatively large inhalable dosages of finely divided SAPL composition may be advantageous when used in combination

with an antiasthma drug, let alone to provide the required reasonable expectation of success. Thus, Mautone does not cure the deficiencies of Radhakrishnan.

To the extent that Mautone concerns doses, Mautone describes a fluorocarbon propellant-based vehicle system for delivery of lipid combinations, arranged to aerosolize an amount of the vehicle sufficient to yield from 210 micrograms to greater than 25mg total lipid per actuation of the aerosol device (Mautone at column 4, lines 4-19). The Mautone systems, however, are aerosolizable suspensions in which the lipid is in a fluorocarbon propellant, rather than in finely divided form. In contrast to Mautone, the present specification stresses the importance of using medicaments in which the lipid is in a finely divided solid form, *i.e.*, a powder (see, *e.g.*, specification at page 2, lines 31-32; page 3, line 31 to page 4, line 5). Mautone does not discuss dosages for administration of a powder.

Importantly, there is nothing in Radhakrishnan and Mautone in combination that would have provided one of ordinary skill in the art with the incentive to consider a therapeutic combination product comprising an antiasthma drug arranged to deliver, in an individual inhalable dosage amount of at least 25mg, or at least 40mg, a medicament comprising a SAPL composition. Radhakrishnan and Mautone, even if properly combined, therefore fail to teach or suggest the invention of claims 1 to 35, and particularly fail to provide a reasonable expectation of success.

Turning to claim 36, the teaching of Radhakrishnan requires that any therapeutic agent will be encapsulated in liposomes. The teaching of Mautone also requires that any therapeutic agent will be incorporated into the lipid crystals there described. Mautone explains that the lipid-drug combination deposits on an aqueous surface at 37°C in the crystalline form "which then instantaneously spreads over the surface as an amorphous surface film carrying with it the therapeutic drug for which it serves as a vehicle" (Mautone at column 3, lines 52-61). Further, it

is clear from the method of manufacture described in Mautone, and recited in all claims thereof, that any drug is to be in intimate association with the lipids.

In contrast to both Radhakrishnan and Mautone, claim 36 requires the drug to be administrable separately from the lipids. Thus, Radhakrishnan and Mautone, even if properly combined, fail to teach or suggest the invention of claim 36. In fact, both Radhakrishnan and Mautone teach away from such an approach, which is clear evidence of patentability. *Mendenhall v. Astec Industries, Inc.*, 13 USPQ2d 1956 (Fed. Cir. 1989).

Regarding claim 37, Radhakrishnan does not teach or suggest combinations of one or more phosphatidyl cholines with a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate. As acknowledged in the Action, Radhakrishnan particularly lacks any teaching on the weight ratios for the components. Mautone describes in general terms and claims compositions with one or more lipids and one or more spreading agents, the lipids being present in an amount of about 80 to 99.5 percent by weight and the spreading agents being present in an amount of about 0.5 to 20 percent by weight.

In contrast, claim 37 requires the ratio of phosphatidyl choline to the second component (selected from phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate) to be from 6:4 to 8:2, SAPL compositions in that range offering effective results in use of the composition of the invention. Although Mautone generally discloses a wide variety of spreading agents, with ratios of 80 to 99.5 percent to 0.5 to 20 percent, including, in addition to various lipids, a wide range of carbohydrates and proteins, there is no teaching or suggestion as to how to limit the 80 to 20 ratios in regard to any particular sub-set of components. There would have been no reason for the skilled artisan, reading Radhakrishnan (which is silent on ratios) and Mautone, to depart from the general teaching of

Mautone to provide a finely divided powder having the specified components and weight ratios of claim 37.

The rejection of all claims under § 103(a) is therefore overcome on various grounds and should be withdrawn.

IV. Rejection of Claims 1, 2 and 6-35 Under 35 U.S.C. § 103(a)

The Action next rejects claims 1, 2 and 6-35 under 35 U.S.C. § 103(a) as allegedly being obvious over PCT publication WO 96/19199 to Byström & Nilsson ("Byström"), taken alone. Although Applicants respectfully traverse, the rejection is overcome.

Claims 3, 4 and 5 are already free from this ground of rejection. As the 6:4 to 8:2 weight ratio of claim 5 is now recited in claim 37, independent claim 37 and dependent claim 24 are also patentable over Byström. The rejection of claims 1, 36 and the dependent claims is also overcome, as set forth below.

Byström is concerned with proliposome powders, and thus with powders adapted to exhibit liposomal behavior when hydrated. Therefore, for analogous reasons to those given above regarding the combination of Radhakrishnan and Mautone, Byström is non-analogous art with respect to the presently claimed invention. In any event, Byström would not teach or suggest the claimed invention to one of ordinary skill in the art.

Claims 1-35 require a finely divided SAPL composition at a relatively high inhalable dose, specified as at least an inhalable amount of 25mg (claim 1) or 40mg (claim 22). Byström does not teach or suggest individual dosage amounts of a finely divided phospholipid composition of at least 25mg. In common with Radhakrishnan, Byström does not recognise any therapeutic effect contributed by the lipid components of their liposomes when hydrated, the lipids being present merely as a delivery vehicle. Thus, there is motivation starting from

Byström for one of ordinary skill in the art to arrive at the doses of claims 1-35, and Byström particularly fails to provide a reasonable expectation of success.

Claim 36 requires that the SAPL composition and the antiasthma drug are provided in a form for separate administration. Byström does not teach or suggest separately administrable phospholipid compositions and antiasthma drugs. In fact, the nature of Byström requires that the therapeutic agent is encapsulated in the resultant liposomes, which teaches away from the invention rather than providing the required suggestion and reasonable expectation of success.

The second rejection of claims 1, 2 and 6-35 under § 103(a) is therefore also overcome and should be withdrawn.

V. Conclusion

This is a complete response to the referenced Official Action. In conclusion, Applicants submit that, in light of the foregoing remarks and enclosed documents, the present case is in condition for allowance and such favorable action is respectfully requested. Should Examiner Haghighatian have any questions or comments, or identify any informalities, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

Shelley P.M. Fussey, Ph.D.
Reg. No. 39,458
Agent for Applicant

WILLIAMS, MORGAN & AMERSON, P.C.
10333 Richmond, Suite 1100
Houston, Texas, 77042
(713) 934-4079

Date: April 02, 2003

EXHIBIT A
PENDING CLAIMS
U.S. SERIAL NO. 09/856,400 (4040.000300)

1. (Twice Amended) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for administration together or separately and the product is arranged for delivery of at least one individual inhalable dose, the individual dose or each individual dose comprising said ingredient (a) in an inhalable amount of at least 25mg.

2. A combination product as claimed in claim 1, in which the ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

3. A combination product as claimed in claim 2, in which medicament (a) comprises said first component and said second component in a weight ratio of from 1:9 to 9:1.

4. A combination product as claimed in claim 3, in which the proportion by weight of said first component exceeds that of said second component.

5. A combination product as claimed in claim 4, in which said first component and said second component are present in a weight ratio of from 6:4 to 8:2.

6. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises a phosphatidyl glycerol.

7. A combination product as claimed in claim 6, in which the phosphatidyl glycerol comprises one or more diacyl phosphatidyl glycerols, of which at least a proportion of the acyl groups are unsaturated.

8. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises one or more compounds selected from the group consisting of diacyl phosphatidyl cholines.

9. A combination product as claimed in claim 8, in which the medicament (a) comprises dipalmitoyl phosphatidyl choline.

10. (Amended) A combination product as claimed in claim 2, in which the medicament (a) is in micronised form.

11. (Amended) A combination product as claimed in claim 2, in which said medicament (a) has a median particle size not exceeding 10μm.

12. A combination product as claimed in claim 11, in which said medicament (a) has a median particle size not exceeding 5μm.

13. A combination product as claimed in claim 12, in which said medicament (a) has a median particle size of less than 3 μm.

14. (Amended) A combination product as claimed in claim 2, in which the antiasthma drug comprises one or more respiratory drugs selected from the group consisting of β_2-agonists, steroids, cromones, antimuscarinic drugs and leukotriene receptor antagonists.

15. (Amended) A combination product as claimed in claim 14, which comprises one or more of said antiasthma drugs in an amount of up to 10 parts by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

16. (Amended) A combination product as claimed in claim 15, which comprises one or more of said respiratory drugs in an amount of up to one part by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

17. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a β_2-agonist.

18. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a steroid.

19. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a cromone.

20. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a leukotriene receptor antagonist.

21. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises an antimuscarinic drug.

22. (Twice Amended) A combination product as claimed in claim 1, wherein the individual dose or each individual dose comprises said ingredient (a) in an inhalable amount of at least 40mg.

23. (Twice Amended) A combination product as claimed in claim 36, wherein the product is arranged for delivery of ingredient (a) in an inhalable amount of at least 25mg.

24. (Twice Amended) A combination product as claimed in claim 37, wherein the product is arranged for delivery of ingredient (a) in an inhalable amount of at least 25mg.

25. (Twice Amended) A combination product as claimed in claim 1, in which at least ingredient (a) is arranged for sequential delivery of a multiplicity of inhalable doses.

26. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery in admixture with ingredient (a).

27. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery separately from, and simultaneously or sequentially with, ingredient (a).

28. (Amended) A pack for use as part of a combination product according to claim 1 or claim 2, said pack including a delivery device for delivery of ingredient (a) to a patient and further comprising instructions to use said delivery device in a method of treatment including the separate simultaneous or sequential administration of an antiasthma drug.

29. (Amended) A method of prevention and/or treatment of asthma, comprising administering to a patient at least one dose of a combination product as defined in claim 1 or claim 2.

30. (Twice Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention and/or treatment of asthma, the delivery device containing a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances the spreading of the medicament, the delivery device being arranged for delivery of at least one individual dose of the SAPL composition in an inhalable amount of at least 25mg.

31. (Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention or treatment of asthma, the delivery device containing a medicament comprising a first component consisting of one or more phosphatidyl cholines and a second component consisting of one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, the delivery device being arranged for delivery of at least one individual inhalable dose, the or each individual dose comprising said first component and said second component in a combined inhalable amount of at least 25mg.

32. (Amended) A delivery device as claimed in claim 30, in which the medicament is as defined in claim 2.

33. (Amended) A delivery device as claimed in claim 30 or 31, which further includes means for dispensing an inhalable dose of an antiasthma drug.

34. (Twice Amended) A medicament for use in the control of asthma, comprising (a) a surface active phospholipid (SAPL) composition in finely divided form conjointly with (b) an antiasthma drug, wherein the medicament is arranged for delivery of said SAPL composition in an individual inhalable dosage amount of at least 25mg.

35. (Amended) A combination product for use in the prevention or treatment of asthma comprising

(a) a medicament comprising a first phospholipid component which is capable of binding to lung tissue and a second component which is capable of enhancing the spreading of said first component over an aqueous medium at 37°C, said medicament being in the form of a finely divided powder; and

(b) an antiasthma drug;

the ingredients (a) and (b) being arranged for administration in combination or separately, simultaneously or sequentially, to deliver ingredient (a) in an individual inhalable dosage amount of at least 25mg.

36. (New) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for separate, simultaneous or sequential, administration and wherein ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

37. (New) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug selected from the group consisting of β_2-agonists, cromones, antimuscarinic drugs and leukotriene receptor antagonists, wherein ingredients (a) and (b) are provided in a form for administration together or in a form for administration separately and wherein ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, said first component and said second component being present in a weight ratio of from 6:4 to 8:2.

EXHIBIT B
PENDING CLAIMS
U.S. SERIAL NO. 09/856,400 (4040.000300)

1. (Twice Amended) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for administration together or separately and the product is arranged for delivery of at least one individual inhalable dose, the individual dose or each individual dose comprising said ingredient (a) in an inhalable amount of at least 25mg.

2. A combination product as claimed in claim 1, in which the ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

3. A combination product as claimed in claim 2, in which medicament (a) comprises said first component and said second component in a weight ratio of from 1:9 to 9:1.

4. A combination product as claimed in claim 3, in which the proportion by weight of said first component exceeds that of said second component.

5. A combination product as claimed in claim 4, in which said first component and said second component are present in a weight ratio of from 6:4 to 8:2.

6. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises a phosphatidyl glycerol.

7. A combination product as claimed in claim 6, in which the phosphatidyl glycerol comprises one or more diacyl phosphatidyl glycerols, of which at least a proportion of the acyl groups are unsaturated.

8. (Amended) A combination product as claimed in claim 2, in which the medicament (a) comprises one or more compounds selected from the group consisting of diacyl phosphatidyl cholines.

9. A combination product as claimed in claim 8, in which the medicament (a) comprises dipalmitoyl phosphatidyl choline.

10. (Amended) A combination product as claimed in claim 2, in which the medicament (a) is in micronised form.

11. (Amended) A combination product as claimed in claim 2, in which said medicament (a) has a median particle size not exceeding 10μm.

12. A combination product as claimed in claim 11, in which said medicament (a) has a median particle size not exceeding 5μm.

13. A combination product as claimed in claim 12, in which said medicament (a) has a median particle size of less than 3 μm.

14. (Amended) A combination product as claimed in claim 2, in which the antiasthma drug comprises one or more respiratory drugs selected from the group consisting of β_2-agonists, steroids, cromones, antimuscarinic drugs and leukotriene receptor antagonists.

15. (Amended) A combination product as claimed in claim 14, which comprises one or more of said antiasthma drugs in an amount of up to 10 parts by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

16. (Amended) A combination product as claimed in claim 15, which comprises one or more of said respiratory drugs in an amount of up to one part by weight per hundred parts by weight of said first and second components of medicament (a) in combination.

17. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a β_2-agonist.

18. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a steroid.

19. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a cromone.

20. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises a leukotriene receptor antagonist.

21. (Amended) A combination product as claimed in claim 14, in which ingredient (b) comprises an antimuscarinic drug.

22. (Twice Amended) A combination product as claimed in [claim 2, in which at least ingredient (a) is arranged to be delivered to a patient in the form of at least one individual inhalable dose, the individual dose or each individual dose comprising said ingredient (a) in an amount of at least 10mg] claim 1, wherein the individual dose or each individual dose comprises said ingredient (a) in an inhalable amount of at least 40mg.

23. (Twice Amended) A combination product as claimed in [claim 22, in which the individual dose or each individual dose comprises said first and second components in a combined] claim 36, wherein the product is arranged for delivery of ingredient (a) in an inhalable amount of at least 25mg.

24. (Twice Amended) A combination product as claimed in [claim 23, in which the individual dose or each individual dose comprises said ingredient (a) in a combined amount of at least 40mg] claim 37, wherein the product is arranged for delivery of ingredient (a) in an inhalable amount of at least 25mg.

25. (Twice Amended) A combination product as claimed in claim [22] 1, in which at least ingredient (a) is arranged for sequential delivery of a multiplicity of inhalable doses.

26. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery in admixture with ingredient (a).

27. (Amended) A combination product as claimed in claim 1 or claim 2, in which the antiasthma drug is arranged for delivery separately from, and simultaneously or sequentially with, ingredient (a).

28. (Amended) A pack for use as part of a combination product according to claim 1 or claim 2, said pack including a delivery device for delivery of ingredient (a) to a patient and further comprising instructions to use said delivery device in a method of treatment including the separate simultaneous or sequential administration of an antiasthma drug.

29. (Amended) A method of prevention and/or treatment of asthma, comprising administering to a patient at least one dose of a combination product as defined in claim 1 or claim 2.

30. (Twice Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention and/or treatment of asthma, the delivery device containing a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances the spreading of the medicament, the delivery device being arranged for delivery of at least one individual dose of the SAPL composition in an inhalable amount of at least [10mg] 25mg.

31. (Amended) A delivery device for administering to a patient by inhalation a medicament for the prevention or treatment of asthma, the delivery device containing a medicament comprising a first component consisting of one or more phosphatidyl cholines and a second component consisting of one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, the delivery device being arranged for delivery of at least one individual inhalable dose, the or each individual dose comprising said first component and said second component in a combined inhalable amount of at least [10mg] 25mg.

32. (Amended) A delivery device as claimed in claim 30, in which the medicament is as defined in claim 2.

33. (Amended) A delivery device as claimed in claim 30 or 31, which further includes means for dispensing an inhalable dose of an antiasthma drug.

34. (Twice Amended) A medicament for use in the control of asthma, comprising (a) a surface active phospholipid (SAPL) composition in finely divided form conjointly with (b) an antiasthma drug, wherein the medicament is arranged for delivery of said SAPL composition in an individual inhalable dosage amount of at least 25mg.

35. (Amended) A combination product for use in the prevention or treatment of asthma comprising

(a) a medicament comprising a first phospholipid component which is capable of binding to lung tissue and a second component which is capable of enhancing the spreading of said first component over an aqueous medium at 37°C, said medicament being in the form of a finely divided powder; and

(b) an antiasthma drug;

the ingredients (a) and (b) being arranged for administration in combination or separately, simultaneously or sequentially, to deliver ingredient (a) in an individual inhalable dosage amount of at least 25mg.

36. (New) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug, wherein ingredients (a) and (b) are provided in a form for separate, simultaneous or sequential, administration and wherein ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate.

37. (New) A therapeutic combination product for use in the prevention and/or treatment of asthma comprising (a) a medicament comprising a surface active phospholipid (SAPL) composition in finely divided form, the SAPL composition including a component which enhances spreading of the medicament over a surface at about normal mammalian body temperature and (b) an antiasthma drug selected from the group consisting of β_2-agonists, cromones, antimuscarinic drugs and leukotriene receptor antagonists, wherein ingredients (a) and (b) are provided in a form for administration together or in a form for administration separately and wherein ingredient (a) consists of a first component comprising one or more phosphatidyl cholines and a second component comprising one or more compounds selected from the group consisting of phosphatidyl glycerols, phosphatidyl ethanolamines, phosphatidyl serines, phosphatidyl inositols and chlorestyl palmitate, said first component and said second component being present in a weight ratio of from 6:4 to 8:2.

said fees from or to Williams, Morgan & Amerson, P.C. Deposit Account No. 50-0786/4040.000300.

Respectfully submitted,

Shelley P.M. Fussey, Ph.D.
Reg. No. 39,458
Agent for Applicants

WILLIAMS, MORGAN & AMERSON, P.C.
10333 Richmond, Suite 1100
Houston, Texas, 77042
(713) 934-4079

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